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REMARKS

Reconsideration of this application, as amended, is respectfully requested.

Consideration and entry of this amendment is respectfully requested as it brings the application into condition for an allowance or in better form for consideration on appeal. The amendment does not raise any substantial new issues that would require any burdensome search by the Examiner.

A. Amendments to the Claims

Claims 44-52 and 73-74 are pending in this application.

Claims 44, 45, 48, 49, 51, 52, 73 and 74 were amended to clarify the invention. Support for all of the amendments can found in the application as originally filed. Accordingly, no new matter has been added to this application as a result of the amendments to the claims.

Claim 45 was amended to replace "HIVI" with "HIV I." Support for this amendment can be found in original claim 56. Claim 45 was also amended to replace "where in" with "wherein" to correct a typographical error. Claims 44, 48, 51 and 52 were amended to clarify the language regarding the third receptor. Support for these amendments can be found at page 5, line 7-9 and page 5, lines 20-23.

Moreover, claims 44, 49 and 51 have also been amended to change the "multicomponent" language back to "multiepitope" to return this terminology back to the terms used in previous versions of the claims and in the originally filed specification. Likewise, references to "analyte-specific components" and "components" in claims 44, 49, 51, 73 and 74 have been changed to "epitope" to return this terminology back to the terms used in previous versions of the claims and in the originally filed specification.

Claims 44 and 49 have been amended to require that a single application of the sample simultaneously contacts the first and second spatially separate test areas. Support for this amendment can be found at page 23, line 5-9.

Claims 44 and 49 have been amended to indicate that a positive test result obtained in one test area is sufficient to indicate the presence of the analyte in said sample. Support for this amendment can be found on page 6, second full paragraph.

Claims 44 and 74 have been amended to change "and" to "or" to clarify the invention. Support for these amendments can be found on page 6, second full paragraph as well as in

Example 2. Page 6 describes the possibility of obtaining a positive test result in only one test area. To obtain a positive test result in only one test area, however, it is necessary to separately determine the presence or amount of the signal generating group bound to either the first or the second test area..

Claims 48, 51 and 52 are amended to clarify the specifically claimed detection reagent. Support for these amendments can be found in the paragraph bridging pages 15-16, where it is disclosed that a digoxigenin-labelled anti-human IgG antibody (the third receptor) directed against the bound p24-specific IgG from the sample is used for the determination of an analyte. Support for a universal detection reagent (anti-digoxigenin labelled latex particles) can be found in Example 1, and at page 23, lines 10-19, page 5, lines 20-24, page 9, lines 6-29 and page 13, lines 23-26.

B. Information Disclosure Statement

The Applicants request that the Examiner execute and return a copy of the PTO 1449 forms for the Information Disclosure Statement mailed May 22, 2001 and Supplemental Information Disclosure Statement mailed September 13, 2005. Copies of PTO stamped acknowledgement postcards are attached as proof that the Patent Office did receive copies of the Statements, PTO 1449 forms and references.

C. Claim Objections

Claim 45 is objected to for use of "HIVI." Claim 45 has been amended to now recite "HIV I" as recommended by the Examiner.

Claim 44 is objected to for the recitation of "one or more third receptors" in part (b) of the claim. The Examiner indicates that the use of "one or more third receptors" in part (b), in combination with the reference to a first and second receptor in part (a) of the claim is confusing. Applicants respectfully disagree that the use of "first," "second" and "third" to modify "receptors" is confusing, as this is how the claims have read for some time. However, in order to expedite prosecution of this application, Applicants have amended claim 44 to read "contacting the sample with the solid phase and with a detection reagent comprising one or more of a third receptor ~~receptors~~" to make clear that a population of a single third receptor is encompassed by the

invention, as opposed to a population of multiple different molecules as the third receptor. Applicants believe that this amendment overcomes the objection. The terms "first", "second" and "third" were used just to number the receptors employed in order to be able to distinguish different receptors. Basically, immobilized receptors are used according to the invention which are bound directly or indirectly to the test areas. In claim 44 (a) said immobilized receptors are referred to as first and second receptor for the purpose of designation only. Further, the invention uses receptors which are not bound to the test area but which bind to the analyte. In order to distinguish these already by their designation from the immobilized receptors referred to as first and second receptors, they are referred to as "third" receptor in claim 44 (b). Said third receptor, thus, is a free receptor which can consist of one or more parts (cf. page 9, 2nd paragraph of the specification).

Finally, claim 44 is objected to for a typographical error. Applicants respectfully submit that the error referenced appears in claim 45, and note that this error has been corrected in the present amendment to the claim.

D. The Claims Are Supported by the Written Description

1. Paragraph 10 of the Office Action Mailed May 30, 2006

Claims 44-52 and 73-74 stand rejected under 35 U.S.C. § 112 for failure to comply with the written description requirement. Applicants respectfully submit that the present amendments to the claims obviate this rejection.

Applicants note that all references in the claims to "multicomponent" have been restored to "multiepitope" and all references to "analyte-specific components" have been restored to "epitopes." These amendments restore these portions of the claim language to the form it was in prior to the last response, and the Office did not find this previous terminology problematic. In light of the present amendments, Applicants respectfully request withdrawal of this written description rejection.

2. Paragraph 11 of the Office Action Mailed May 30, 2006

Claim 49 stands further rejected under 35 U.S.C. § 112 for failure to comply with the written description requirement. Applicants respectfully submit that the amendments made to claim 49 render this rejection moot.

Thus, Applicants respectfully request withdrawal of the rejection of claims 49 under 35 U.S.C. § 112 for failure to comply with the written description requirement.

3. Paragraph 12 of the Office Action Mailed May 30, 2006

Claims 48 and 52 stand further rejected under 35 U.S.C. § 112 for failure to comply with the written description requirement. Applicants respectfully submit that the present amendments to the claims 48 and 52 obviate this rejection.

The Office asserts that no support could be found in the specification for the recitation of a "signal-generating reagent" and that the specification only supports a "signal-generating group" that is bound to the third receptor. The claims as amended recite a "signal-generating group" that is bound to the third receptor. Thus, Applicants respectfully request withdrawal of this rejection.

4. Paragraph 13 of the Office Action Mailed May 30, 2006

Claim 74 further stands rejected under 35 U.S.C. § 112 for failure to comply with the written description requirement. Applicants respectfully traverse this rejection.

The Office asserts that no support can be found for a generic disclosure of the use of a test area-specific cut-off value in the application at p. 10-11. However, the use of a test area-specific cut-off value is literally described on page 11, first full paragraph. While Applicants do not agree that this portion of the specification does not support claim 74, Applicants additionally point the Office to page 21, lines 12-31 as support for claim 74. At page 21, the specification describes the use of a test area-specific threshold value (indistinguishable from the claimed cut-off value) in a method for detection of an analyte. Applicants submit that page 21 provides a generic disclosure of the use of a test area-specific cut-off value in the methods of the invention. Thus, Applicants respectfully request withdrawal of this rejection.

E. <u>The Claims Are Not Indefinite</u>

1. Paragraph 16 of the Office Action Mailed May 30, 2006

Claims 44-52 and 73-74 stand rejected under 35 U.S.C. § 112, second paragraph for failure to comply with the definiteness requirement for the use of the term "analyte." The Office

asserts that Applicants are using "analyte" in a non-standard way without putting one of skill of art on notice that the Applicant intended to redefine the term. Applicants respectfully disagree. Applicants use of "analyte" is clarified by reference to page 5, last paragraph to page 6, line 5. To clearly redefine a term, Applicants are not required to specifically identify a new definition for the term. All that is required is that one of skill in the art recognize that a non-standard definition is intended by the Applicant. The cited language at pages 5-6 clearly puts one of skill in the art on notice of Applicants intended use of the term analyte. Therefore, Applicants respectfully request withdrawal of this rejection.

2. Paragraphs 17-19 of the Office Action Mailed May 30, 2006

Claims 44, 49, 51 and 73-74 stand rejected under 35 U.S.C. § 112, second paragraph for failure to comply with the definiteness requirement for the use of the terms "multicomponent" and "analyte-specific components." In light of the claim amendments removing these terms from the claims, Applicants respectfully request withdrawal of these rejections.

F. The Claims Are Not Anticipated by Linsley *et al.*

Claims 44, 47, 49, 51 and 74 stand rejected under 35 U.S.C. § 102(e) as being unpatentable over Linsley et al., U.S. Patent No. 6,004,761 (hereinafter "Linsley"). Applicants respectfully submit that Linsley fails to teach all of the limitations of the rejected claims and thus, cannot anticipate these claims.

As noted previously, Linsley describes new monoclonal antibodies reactive with mucins, and the individual binding of these antibodies to mucins is described using a double determinant immunoassay (DDIA). Linsley describes an assay in which a first antibody is immobilized on a solid phase, then treated with the sample and thereafter bound with a second antibody which is labelled (cf. column 3, line 66 to column 4, line 17). The designation "double determinant", thus, refers to the use of two antibodies in the sense of a sandwich assay for the detection of an analyte, whereby one determinant is used for binding to a solid phase via a first antibody and a second determinant for attaching a label via a second antibody. Further, it is stated that the second labeled antibody, if necessary, should also bind to a different epitope than the first antibody (cf. column 4, lines 17-30).

Applicants respectfully submit that Linsley does not teach a single solid phase with at least a first and a second receptor, the first and second receptors binding specifically with said analyte but to different epitopes (claim 44) or a single solid phase with a first and a second receptor, the receptors binding specifically to the analyte but to different epitopes of the analyte (claim 49). Specifically, Applicants read the Examples in Linsley as describing experiments where only one antibody is immobilized on a solid phase, e.g. Onc-M26 or Onc-M29 (cf. column 17, line 58), as capture antibody. Applicants' interpretation of the Examples is further supported by claim 3, which describes the binding of only a single capture antibody to the substrate. In other words, Applicants read Linsley as teaching that multiple different tests are carried out on multiple different plates (solid phases) whereas in the present invention, parallel or simultaneous detection of multiple epitopes of an analyte is accomplished in a single test. Consequently, Applicants' believe that simultaneous detection of multiple epitopes of an analyte by different immobilized receptors specific for different epitopes is not disclosed in Linsley.

Although Applicants disagree that Linsley teaches the method of claim 44 and the solid phase of claim 49 as present in the last submission, Applicants have amended claims 44 and 49 to make clear that only a single application of the sample (for example, a single pipetting of the sample) is used to contact the solid phase, such that the single application of the sample simultaneously contacts the first and second spatially separate test areas. This new limitation is clearly not taught by Linsley, which expressly states that samples were "pipetted onto duplicate coated wells" (col. 18, lines 18-19). Pipetting into multiple wells is not a single application of the test sample. Moreover, since the wells in Linsley as physically separated from each other, the single application of the sample to the solid phase cannot simultaneously contact the first and second spatially separate test areas. Thus, Linsley does not anticipate amended claims 44 and 49. Because Linsley does not teach all of the limitations of claims 44 or 49, Linsley cannot anticipate claim 44, 49 or dependent claims 47, 51 and 74. Therefore, Applicants respectfully request withdrawal of the rejection.

G. The Claims Are Not Anticipated by Fleming

Claim 49 stands rejected under 35 U.S.C. § 102(b) as being unpatentable over Fleming, U.S. Patent No. 5,149,626 (hereinafter "Fleming"). However, Fleming does not disclose that a

positive test result obtained in one test area is sufficient for indicating the presence of an analyte in a sample, as required by claim 49 as presently amended. Thus, Fleming does not teach each element of claim 49 as amended and therefore, does not anticipate claim 49 as amended. In light of the amendments to claim 49, Applicants respectfully request withdrawal of this rejection.

H. The Claims Are Not Obvious from Ekins *et al.* in view of Schonbrunner

Claims 44-46, 48-52 and 73 stand rejected under 35 U.S.C. § 103 as being unpatentable over Ekins, U.S. Patent No. 5,516,638 (hereinafter "Ekins"), in view of Schonbrunner, UK Patent Application Publication GB 2313 666 A (hereinafter "Schonbrunner"). Applicants respectfully traverse the rejection.

A claimed invention is unpatentable if the differences between it and the prior art "are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." 35 U.S.C. § 103(a); *see Graham v. John Deere Co.*, 383 U.S. 1, 14 (1966). The ultimate determination of whether an invention is or is not obvious is based on underlying factual inquiries including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the prior art; (3) the differences between the claimed invention and the prior art; and (4) objective evidence of nonobviousness. *See Graham*, 383 U.S. at 17-18.

The MPEP clearly provides the criteria for establishing a *prima facie* case of obviousness: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP § 2142. The obviousness inquiry set forth in *Graham* focuses on whether the prior art as a whole teaches, suggests, or motivates one of ordinary skill in the art to make the invention and whether the skilled artisan would have a reasonable expectation of making and using it. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). The suggestion, teaching, or motivation to combine may flow from the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. *See Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573 (Fed. Cir. 1996).

In this case, the Office has not shown that the references or the knowledge generally available to one of ordinary skill in the art provide any suggestion or motivation to modify the reference or to combine reference teachings. Thus, Applicants respectfully submit that the Office has failed to establish a *prima facie* case of obviousness as the rejected claims. Applicants also submit that the Office establish cannot a *prima facie* case of obviousness of these claims in view of the present amendments to claims 44 and 49 because the references fail to teach or suggest all of the elements of the amended claims.

The Office concedes that Ekins fails to specifically teach different receptors bound to different test areas which are specific for different epitopes. While Schonbrunner does teach the use of different receptors which are specific for different epitopes, Schonbrunner does not teach that these receptors are bound to different test areas. Instead, Schonbrunner's teaches the detection of an analyte by different epitopes in a mixture; thus, the epitope-specific evaluation of the present invention is not possible using the methods and solid phases of Schonbrunner. Although Ekins and Schonbrunner may teach the various elements of claims 44 and 49, the Office has not identified any suggestion or motivation to combine the elements taught by Ekins with the elements taught by Schonbrunner. For example, nowhere in the references is there any suggestion that higher sensitivity may be achieved by using the multi-component detection of Schonbrunner with the separate test areas of Ekins. In the absence of any suggestion or motivation to combine, Applicants respectfully submit that the Office has engaged in an impermissible hindsight reconstruction of the claimed invention. Because the Office has shown no motivation to combine Ekins with Schonbrunner to arrive at all of limitations of independent claims 44 and 49, Applicants respectfully submit that these claims are not obvious. Further, according to the present invention, a positive test result obtained in one test area is sufficient to indicate the presence of the analyte in the sample. A procedure and identification like that, however, is not possible at all either by the method of Schonbrunner or by the method of Ekins.

Claims 45, 46, 48 and 73 depend from claim 44 and claims 51 and 52 depend from claim 49. Because the Office has shown no motivation to combine Ekins with Schonbrunner to arrive at all of limitations of independent claims 44 and 49, Applicants respectfully submit that these dependent claims are also not obvious.

Moreover, Applicants respectfully submit that the references do not provide a motivation to combine the elements of Ekins with the clements to Schonbrunner to arrive at the all of the

elements of claims 44 and 49 as presently amended. Thus, Applicants respectfully request withdrawal of the rejection.

I. The Claims Are Not Obvious from Ekins *et al.*, Schonbrunner and O'Conner

Claims 47 and 74 stand rejected under 35 U.S.C. § 103 as being unpatentable over Ekins, in view of Schonbrunner, and in further view of O'Conner *et al.*, U.S. Patent No. 5,627,026. Claims 47 and 74 both depend from independent claim 44. For the same reasons discussed above for the rejection of claim 44 over Ekins in view of Schonbrunner, Applicants respectfully traverse the rejection. As noted above, the Office has failed to make out a prima facie case of obviousness because the Office has failed to point out any motivation or suggestion to combine the teachings of Ekins with Schonbrunner. Likewise, the Office has failed to point out any motivation or suggestion to combine the teachings of Ekins, Schonbrunner and O'Conner. Nothing in O'Conner (or the other references) suggests the desirability of combining its teaching of control areas with the teachings of either Schonbrunner or Ekins. Nor does O'Conner teach or suggest combining its teachings with Schonbrunner or Ekins. O'Connor is also silent with regard to the fact that the presence of an analyte in a sample can be indicated when a positive signal is produced in one test area.

In the absence of any suggestion or motivation to combine, Applicants respectfully submit that the Office has engaged in an impermissible hindsight reconstruction of the elements of claim 47. Because the Office has shown no motivation to combine Ekins with Schonbrunner and O'Conner to arrive at all of limitations of claims 47, Applicants respectfully submit that these claims are not obvious and request withdrawal of the rejection.

J. The Claims Are Not Obvious from Linsley *et al.* in view of Ekins *et al.*

Claims 45, 48, 50 and 52 stand rejected under 35 U.S.C. § 103 as being unpatentable over Linsley in view of Elkins *et al.*. Applicants respectfully traverse these rejections.

For the reasons discussed above in the anticipation rejection based on Linsley, Applicants respectfully submit that Linsley fails to teach all of the limitations of the underlying independent claims (claims 44 and 49) as present in the last submission.

Moreover, in light of the present amendments to the underlying independent claims, Linsley does not teach all of the elements of claims 44 and 49. As discussed above, Linsley does not teach that the only a single application of the sample (for example, a single pipetting of the sample) is used to contact the solid phase, such that the single application of the sample simultaneously contacts the first and second spatially separate test areas. Nothing in Ekins teaches or suggests this limitation either.

Without a teaching of all of the claimed elements in the underlying independent claims 44 and 49, the obviousness rejection of claims 45, 48, 50 and 52 cannot stand.

K. Double Patenting

Claims 44-52 and 73-74 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of U.S. Patent No. 6,815,217.

The subjects of U.S. Patent No. 6,815,217 and the present application are basically different. U.S. 6,815,217 concerns the use of control spots, by means of which non-specific binding events can be determined and, thus, an analytical result can be improved. In contrast thereto, the core of the present invention does not relate to control spots but rather to multiepitope analysis. Control spots can only additionally be used. In view of the differences between the present application and claim 1-34 of U.S. Patent No. 6,815,217, Applicants respectfully request that the double patenting rejection be withdrawn.

L. Conclusion

In view of the amendments and remarks above, the application is considered to be in proper form for allowance. Therefore, the Office is respectfully requested to pass the application to issue. If the Office is of the opinion that a teleconference would expedite the prosecution of the application, the Examiner is encouraged to contact Applicant's undersigned representative.

Reconsideration of this application is respectfully requested and a favorable determination is earnestly solicited. The Examiner is invited to contact the Applicants' undersigned representative at (312) 913-2126 if the Examiner believes that this would be helpful in expediting prosecution of this application.

Date: November 29, 2006

Respectfully,

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Hon. Commissioner of Patents & Trademarks
Re: Applicant - Karl, Johann et al.
Title: "Improvement of Binding Assays by Multiepitope Analysis and by Combining Antigen and Antibody Determination"
Case No. 05-042

Atty: EMVnc
U.S.S.N. 09/720,006

Sir:

Please place the Patent Office receipt stamp hereon and mail to acknowledge receipt of the following:

☒ Transmittal Letter (1 sheet);
☒ First Supplemental Information Disclosure Statement (IDS) (2 sheet);
☒ Form PTO-1449 (1 sheet); and
☒ 6 cited references.

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Date Mailed: September 13, 2005

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Respectfully,
McDonnell Boehnen Hulbert & Berghoff LLP
Attorneys for Applicant

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FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 05-042	Serial No. 09/720,006
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) COPY		Applicant: Karl, Johann et al.	
		Filing Date: December 19, 2000	Group: 1641

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	1	5,627,026	05/06/1997	O'Connor et al.	435	5	

FOREIGN PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Country	Class	Subclass	Translation Yes	Translation No
	2	0 461 462 A1	12/18/1991	Europe				
	3	WO 93/08472	04/29/1993	PCT				
	4	WO 97/32212	09/04/1997	PCT				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc).

	5	R. Ekins et al., "Multianalyte microspot immunoassay. The microanalytical "compact disk" of the future.", *Annales De Biologie Clinique*, Vol. 50, Nr. 5, 1992, pp. 337-353
	6	R. Ekins et al., "Development of microspot multi-analyte ratiometric immunoassay using dual fluorescent—labelled antibodies.", *Analytica Chimica ACTA*, Vol. 227, Nr. 1, pp. 73-96, December 1, 1989.
	7	S.E. Kakabakos et al., "Multianalyte immunoassay based on spatially distinct fluorescent areas quantified by laser-excited solid-phase time-resolved fluorometry", *Clinical Chemistry*, Vol. 38, Nr. 3, March 1992, pp. 338-342.
EXAMINER		DATE CONSIDERED	

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

INFORMATION DISCLOSURE CITATION
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ATTY DOCKET NO.	SERIAL NO.
RDID0011	09/720,006
KARL, Johann, et al.	
FILING: December 19, 2000	GROUP: To Be Assigned

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	1	5,627,026	05/97	O'Conner et al.	435	5	

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO
	2	EP0351248B1	01/90	Europe	G01N	33/53		
	3	EP0445423A2	09/91	Europe	G01N	33/576		
	4	EP0445423B1	09/91	Europe	G01N	33/576		
	5	EP0461462A1	12/91	Europe	G01N	33/543		

OTHER DOCUMENTS *(Including Author, Title, Date, Pertinent Pages, Etc.)*

EXAMINER	DATE CONSIDERED

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Inventors: KARL, Johann, et al.
Serial No.: 09/720,006
Filing Date: December 19, 2000
Entitled: IMPROVEMENT OF BINDING ASSAYS BY MULTIEPITOPE ANALYSIS AND BY COMBINING ANTIGEN AND ANTIBODY DETERMINATION
Our Ref. No.: RDID00115

Enclosures: Transmittal of Information Disclosure Statement (2pgs) page 2 in duplicate, Information Disclosure Citation (1pg), Copies of references listed thereon, and return postcard

Mailed Via First Class Mailed on May 17, 2001

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